

*REMARKS/ARGUMENTS**The Pending Claims*

Claims 36, 37, and 40-70 are pending and are directed to a bacterial artificial chromosome (BAC) and a method of producing and mutagenizing same.

The Office Action

Claims 36, 37, and 40-70 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Messerle et al., *J. Mol. Med.*, 74: B8 (1996) ("the Messerle reference") and Chartier et al., *J. Virol.*, 70: 4805-4810 (1996) ("the Chartier reference") alone or in combination with one or more of the following secondary references: Ehtisham et al., *J. Virol.*, 67: 5247-5252 (1993) ("the Ehtisham reference"), Gage et al., *J. Virol.*, 66: 5509-5515 (1992) ("the Gage reference"), Chen et al., *Mol. Cell. Biol.*, 7: 2745-2752 (1987) ("the Chen reference"), and Luckow et al., *J. Virol.*, 67: 4566-4579 (1993) ("the Luckow reference"). Reconsideration of these rejections is respectfully requested.

Discussion of Rejections Under 35 U.S.C. § 103

Claims 36, 37, and 40-70 have been rejected under Section 103 as allegedly unpatentable over the combination of the Messerle reference and the Chartier reference alone or in combination with one or more secondary references. This rejection is traversed for the reasons set forth below.

For subject matter defined by a claim to be considered obvious, the Office must demonstrate that the differences between the claimed subject matter and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a); see also *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). The ultimate determination of whether an invention is or is not obvious is based on certain factual inquiries including: (1) the scope and content of the prior art, (2) the level of ordinary skill in the prior art, (3) the differences between the claimed invention and the prior art, and (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17-18, 148 U.S.P.Q. at 467.

Consideration of the aforementioned Graham factors here indicates that the present invention, as defined by the pending claims, is unobvious in view of the cited references.

Regarding the scope and content of the prior art, the Messerle reference discloses reconstituting two BAC/MCMV hybrid plasmids in eukaryotic cells that do not contain any herpes virus genes or herpes virus proteins. The Chartier reference discloses the assembly of an entire adenovirus genome via plasmid recombination in *E. coli*.

For the sake of argument and for purposes of the present analysis, one of ordinary skill in the art can be assumed to be someone with an advanced degree and a few years of experience in the relevant art.

With respect to the differences between the claimed invention and the cited references, Applicants note that the Messerle reference does not disclose a BAC containing all genes essential for the generation of an infectious herpes virus in a host cell, wherein the host cell does not contain any herpes virus genes or herpes virus proteins. The Chartier reference differs from the claimed invention in several respects. In particular, the Chartier reference discloses assembling a 36 kb adenovirus genome in *E. coli*, which is considerably smaller than the size of the herpes virus genome as presently claimed. Secondly, the Chartier reference discloses using plasmids, not BACs, for assembling adenovirus genomes. The Chartier reference discloses plasmid recombination in *E. coli*, while the claimed BAC is produced by recombination in eukaryotic cells.

Contrary to the assertions of the Office Action, one of ordinary skill in the art would not have even considered the Chartier reference to compensate for the deficiencies of the Messerle reference. In this respect, Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 of Martin Messerle, which demonstrates that the method of assembling an adenovirus genome disclosed in the Chartier reference is not suitable for generating virus genomes that are larger than an adenovirus genome (i.e., larger than 36 kb). The Rule 132 declaration also demonstrates that, even if one of ordinary skill in the art were motivated to combine the the Messerle reference and the Chartier reference, such combination does not provide a reasonable expectation of success in arriving at the claimed invention.

Applicants also remind the Office that “[i]f the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 U.S.P.Q. 349 (C.C.P.A. 1959).” (M.P.E.P. § 2143.01). As discussed in the Rule 132 declaration, combining the Messerle reference and the Chartier reference to arrive at the claimed invention would require changing the principle operation of those references. Specifically, the *E. coli* strain and plasmids used in the recombination experiments of the Chartier reference would not support the large viral genomes disclosed in the Messerle reference. Moreover, the Examiner’s contention that “the method of Chartier et al. is further applicable to any large virus genome” (Office Action at page 4, last paragraph) is simply untrue. There is nothing in any of the cited references to corroborate this statement, and the Office Action has provided no other evidence to support this assertion.

None of the secondary references cited by the Office Action compensates for the deficiencies of the Messerle reference. In this respect, none of the Ehtisham, Gage, Chen, and Luckow references discloses or suggests a BAC containing all genes essential for the generation of an infectious herpes virus in a host cell, wherein the host cell does not contain any herpes virus genes or herpes virus proteins.

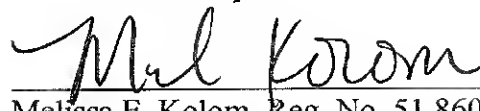
For purposes of considering the obviousness rejections, there is no need to consider any objective evidence of nonobviousness.

Considering all of the Graham factors together, it is clear that the present invention would not have been obvious to one of ordinary skill in the art at the relevant time in view of the combination of cited references. Accordingly, the obviousness rejections under Section 103 should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,

A handwritten signature in cursive script, reading "Mel Kolom". The signature is written in black ink and is positioned above a horizontal line.

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